IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

UNITED THERAPEUTICS CORPORATION, Plaintiff, v. LIQUIDIA TECHNOLOGIES, INC., Defendant.	)	C.A. No. 23-975-RGA-SRF

DEFENDANT'S POST-TRIAL OPENING BRIEF REGARDING INVALIDITY OF U.S. PATENT NO. 11,826,327

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Asserted Patents & Parties

’327 patent or ’327	U.S. Patent No. 11,826,327
Asserted Claims	Claims 1, 5, 6, 9, 14, 17 of U.S. Patent No. 11,826,327
Liquidia or Defendant	Liquidia Technologies, Inc.
UTC or Plaintiff	United Therapeutics Corporation

Commonly Used Terms & Abbreviations

’793 patent	U.S. Patent No. 10,716,793 (DTX2)
’507 patent	U.S. Patent No. 9,339,507 (DTX62)
2018 Earnings Call	United Therapeutics Corporation FQ1 2018 Earnings Call Transcript, (May 2, 2018) (DTX3)
6MWD	Six-minute walk distance
6MWT	Six-minute walk test
Agarwal	M. Agarwal and A.B. Waxman, *Inhaled Treprostinil in Group-3 Pulmonary Hypertension*, J. Heart and Lung Transplant. 34(4):S343 (2015) (DTX161)
BNP	B-type natriuretic peptide
CPFE	Combined pulmonary fibrosis and emphysema
DPI	Dry powder inhaler
Dr. Channick	Richard Channick, M.D.
Dr. Hill	Nicholas Hill, M.D.
Dr. Nathan	Steven Nathan, M.D.
Dr. Saggar	Rajan Saggar, M.D.
Dr. Tapson	Victor Tapson, M.D.
Dr. Thisted	Ronald Thisted, Ph.D.
Dr. Waxman	Aaron Waxman, M.D.
Dr. Wertheim	Bradley Wertheim, M.D.
Faria-Urbina	M. Faria-Urbina, et al., *Inhaled Treprostinil in Pulmonary Hypertension Associated with Lung Disease*, Lung 196:139–146 (2018) (DTX348) (Supplementary Materials at DTX505)
FDA	Food and Drug Administration
FVC	Forced Vital Capacity
FOF	Findings of Fact related to Invalidity of U.S. Patent No. 11,826,327
HRCT	High-resolution computed tomography
IIP	Idiopathic interstitial pneumonia
ILD	Interstitial lung disease
INCREASE	A Multicenter, Randomized, Double-Blinded, Placebo-Controlled Trial to Evaluate the Safety and Efficacy of

TABLE OF ABBREVIATIONS

	Inhaled Treprostinil in Subjects With Pulmonary Hypertension Due to Parenchymal Lung Disease
IPF	Idiopathic pulmonary fibrosis
IPR	*Inter partes review*
iTre	Inhaled treprostinil
ITT population	Intent-to-treat population (ie all patients in INCREASE)
IV	Intravenous
Mcgs	Micrograms
mPAP	Mean pulmonary artery pressure
NDA	New Drug Application
NEJM Paper	A. Waxman, et al., *Inhaled Treprostinil in Pulmonary Hypertension Due to Interstitial Lung Disease*, N. Eng. J. Med. 384(4):325 (2021) (DTX363)
NT-proBNP	N-terminal pro b-type natriuretic peptide
Parikh	Kishan Parikh et al, *Safety and Tolerability of High-dose Inhaled Treprostinil in Pulmonary Hypertension*, 67 J. Cardiovascular Pharmacology 322-25 (2016) (DTX51)
PAH	Pulmonary arterial hypertension (Group 1 PH)
PAWP	Pulmonary artery wedge pressure
PCWP	Pulmonary capillary wedge pressure
PF	Pulmonary fibrosis
PFT	Pulmonary function test
PH	Pulmonary hypertension
PH-ILD or ILD-PH	Pulmonary hypertension associated with interstitial lung disease (Group 3 PH)
POSA	Person of ordinary skill in the art
PTAB	Patent Trial and Appeal Board
PVR	Pulmonary vascular resistance
RHC	Right heart catheterization
Saggar 2014	Saggar, R., et al., *Changes in right heart haemodynamics and echocardiographic function in an advanced phenotype of pulmonary hypertension and right heart dysfunction associated with pulmonary fibrosis*, Thorax 2014;69:123–129 (2014) (DTX10)
USPTO or PTO	United States Patent and Trademark Office
V/Q	Ventilation/perfusion
WHO	World Health Organization
WU	Wood unit

I. INTRODUCTION

"This drug works." That's what UTC's CEO told the public in 2018 when discussing the use of Tyvaso to treat PH-ILD patients. How did UTC know this? Because since 2009, doctors treated PH-ILD patients with Tyvaso sold to those patients, using the identical dosing in claim 1 of the '327 patent, published their successful results in peer reviewed journals, presented data at conferences, and told UTC back in 2015 to confirm these results in a larger study, leading to INCREASE. Now, however, based on the data from a clinical trial conceived of and designed by individuals other than the named inventors, UTC obtained the '327 patent and has taken from the public the identical method of treating PH-ILD patients with inhaled treprostinil ("iTre") that was being continually practiced for the last decade. The trial record, summarized here and in Liquidia's accompanying FOF, establishes by clear and convincing evidence that the Asserted Claims of the '327 patent are invalid under §§ 102, 103 and 112. FOF4.

II. FACTUAL BACKGROUND

Please see Defendant's Findings of Fact Related to Invalidity of the '327 patent.

III. CLAIMS 5, 6, 9 AND 17 ARE NOT ENTITLED TO PATENTABLE WEIGHT

The Court need not address the validity of dependent claims 5, 6, 9 and 17 because they have no patentable weight. When the language of a method of treatment "is only a statement of purpose and intended result[,]" and "does not result in a manipulative difference in the steps of the claim[s,]" such claim language is nonlimiting and has no patentable weight. *Bristol-Myers Squibb Co. v. Ben Venue Lab'ys, Inc.*, 246 F.3d 1368, 1375-76 (Fed. Cir. 2001) ("*BMS*"); *see also In re Copaxone Consol. Cases*, 906 F.3d 1013, 1023 (Fed. Cir. 2018); *Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 2023 WL 11891335, at *11-13 (N.D. W. Va. Apr. 19, 2023). Claims directed to intended results are "generally not considered to be claim limitations where the 'method [is] performed in the same way regardless whether or not the [intended result actually ensues] . . . .'"

Takeda Pharm. Co. v. Actavis Lab'ys FL, Inc., 2016 WL 3193188, at *7 (D. Del. June 6, 2016) (alteration in original) (citing *BMS*, 246 F.3d at 1375). This analysis applies to both independent and dependent claims. *See Regeneron*, 2023 WL 11891335, at *11-13. Here, dependent claims 5, 6, 9, and 17 have no patentable weight because they merely recite the intended results of performing the method of independent claim 1. FOF9.

A. Claims 5, 6, 9 and 17 Are Directed to the Intended Results of Claim 1

Dr. Nathan testified claims 5, 6, 9, and 17 are directed to the intended result of the dosing and administration recited in claim 1. FOF7, 9. Dr. Nathan testified that none of the claimed outcomes need to be measured for direct infringement. *Id*. And for claims 6 and 9, a doctor does not need to assess whether the claimed statistically significant results actually occurred. *Id*. In fact, "the patient doesn't need to actually achieve the outcomes in 5, 6, 9, or 17 to infringe," because they are "automatically" infringed if claim 1 is practiced. FOF9-10.

Because claims 5, 6, 9 and 17 are only directed to intended results, and no further step is needed to infringe these claims, the same interpretation is required for invalidity and they are not entitled to patentable weight. *See BMS*, 246 F.3d at 1376; *In re Copaxone*, 906 F.3d at 1023; *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1351 (Fed. Cir. 2001). Accordingly, claims 5, 6, 9 and 17 cannot bear on the validity of the '327 patent and would be invalid if claim 1 is found invalid. *See Bristol-Myers Squibb Co. v. Boehringer Ingelheim Corp.*, 86 F. Supp. 2d 433, 442 (D.N.J. 2000), *aff'd in part, vacated in part sub nom., Bristol-Myers Squibb Co. v. Ben Venue Lab'ys, Inc.*, 246 F.3d 1368 (Fed. Cir. 2001) (holding non-limiting preamble language did not factor into the validity analysis, and even if the language were limiting, prior art producing the same result anticipated the claim).

B. Claims 5, 6, 9 and 17 Do Not Manipulate the Method of Claim 1

Claims 5, 6, 9 and 17 do not lead to manipulative differences in performing claim 1. Dr.

Nathan confirmed these claims are "automatically" infringed if claim 1 is practiced. FOF10. Thus, all the claims are performed by a single step of treating a PH-ILD patient with iTre at the claimed dosing. *See Takeda Pharm.*, 2016 WL 3193188, at *7.

UTC cannot contend that claims 5, 6, 9 and 17 provide a manipulative difference because, allegedly, only certain formulations of iTre may infringe.[1] The data underlying claims 5, 6, 9 and 17 is from INCREASE (FOF5), which used Tyvaso, not Yutrepia—two completely different formulations of iTre. Tr. 135:12-20. UTC nonetheless asserted that INCREASE, alone, proves infringement. Dr. Nathan speculated that if Pfizer developed a "different formulation" of iTre, claims 5, 6, 9 and 17 may not be infringed even if dosed according to claim 1 and Pfizer product data would be needed to determine infringement. Tr. 162:23-164:7. This speculation cannot be reconciled with his opinion that Yutrepia, also a "different formulation," automatically infringes based solely on INCREASE. Tr. 135:9-137:1. Claims 5, 6, 9 and 17 do not change the execution of claim 1 and, even under the Pfizer example, they are not afforded patentable weight for purposes of validity.

L'Oréal USA, Inc. v. Olaplex, Inc., 844 F. App'x 308, 313 (Fed. Cir. 2021), does not save the claims because that case involved a claim that required performance of a comparison step between a bleaching formulation *with* and *without* the claimed "active agent." By contrast, Dr. Nathan says claims 5, 6, 9 and 17 require no additional steps to be taken beyond those set forth in claim 1. FOF9. For these reasons, claims 5, 6, 9 and 17 are directed to intended results, have no patentable weight, and cannot be relied upon by UTC to establish the validity of the '327 patent.

[1] Even if the intended results of claims 5, 6, 9 and 17 do not always occur, that does not grant claims patentable weight. *See Takeda Pharm.*, 2016 WL 3193188, at *7.

IV. THE ASSERTED CLAIMS OF THE '327 PATENT ARE INVALID UNDER § 103

Obviousness requires a POSA to "have been motivated to combine the teachings of the prior art references to achieve the claimed invention [with a] reasonable expectation in doing so." *Hospira, Inc. v. Amneal Pharms., LLC*, 285 F. Supp. 3d 776, 784 (D. Del. 2018), *aff'd*, 748 F. App'x 1024 (Fed. Cir. 2019). The evidence establishes that the Asserted Claims are obvious in view of combinations of *Faria-Urbina*, the '793 patent, and *Saggar 2014*. Testimony from practicing POSAs, prior art, UTC's documents, and statements by UTC's CEO, years before April 2020, demonstrate there was ample motivation to treat PH-ILD patients with iTre and a reasonable expectation that such treatment would succeed in achieving the outcomes of the Asserted Claims.

A. The '793 Patent Is Prior Art

Liquidia met its burden that the '793 patent is prior art under 35 U.S.C. §102(a)(2) because the '793 and '327 patents name different inventors (*compare* DTX2, *with* JTX1), claim priority back to 2006, and the original non-provisional application that led to the '793 patent was effectively filed on May 14, 2007, years before UTC's claimed April 17, 2020 effective filing date for the '327 patent (*compare* DTX2, 1, *with* JTX1, 1). FOF11-12. Other than UTC's §102(b)(2)(C) challenge based on common ownership, UTC does not dispute that the '793 patent qualifies as §102(a)(2) prior art.

1. The §102(b)(2)(C) Exception Does Not Apply

Once Liquidia showed that the '793 patent qualified as prior art under §102(a)(2), the burden shifted to UTC to show the §102(b)(2)(C) exception applied, as stated in the Joint Pretrial Order. D.I. 335 Ex. 17, ¶¶15, 17; *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1379-80 (Fed. Cir. 2015) (after patent challenger establishes initial burden of production that the reference is prior art, the burden of production shifts to patent owner to produce evidence that it does not qualify as prior art). To rely on the (b)(2)(C) exception, UTC must "produc[e]

additional evidence and present[] persuasive argument" establishing "not later than the effective filing date of the claimed invention," both patents "were owned by the same person or subject to an obligation of assignment to the same person." 35 U.S.C. §102(b)(2)(C); *see Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1315, 1327-29 (Fed. Cir. 2008). UTC established neither.

UTC offered no evidence establishing that any inventor was "subject to an obligation" to assign any rights in the '793 or '327 patents prior to the effective filing date of the '327 patent. FOF13-16. Dr. Noah Byrd, UTC's VP for Global Regulatory Affairs, did not testify about any obligation to assign patents to UTC. Tr. 29:15-30:3. The mere fact that some '327 patent inventors may have been UTC employees does not establish an obligation to assign. *Bd. of Trustees Trs. of the Leland Stanford Jr. Univ. v. Roche Molecular Sys.*, 563 U.S. 776, 786 (2011) ("unless there is an agreement to the contrary, an employer does not have rights in an invention 'which is the original conception of the employee alone.'" (quoting *U.S. v. Dubilier Condenser Corp.,* 289 U.S. 178, 189 (1933))). UTC also offered no evidence that any named inventor of the '793 patent was a UTC employee or had any obligation to assign their patent rights. FOF13. Thus, it is no surprise that UTC only attempted to address common ownership under (b)(2)(C). PDX8, 10.

But UTC failed to provide evidence that it actually owned the full rights to the '793 and '327 patents ***prior to*** the effective filing date of the '327 patent. FOF13-16. Dr. Byrd provided UTC's only testimony on patent ownership. Based only on his "high level" knowledge from patents listed in the Orange Book and with merely a "high level" awareness that UTC even listed such patents, he stated that UTC "currently owns" and "always owned the issued patents" listed for Tyvaso in the Orange Book "from the date each one was first filed." *See* Tr. 35:14-36:24.

Dr. Byrd's conclusory testimony fails to meet UTC's burden of establishing common ownership as of the April 2020 priority date. *See Dynamic*, 800 F.3d at 1381-82 (affirming

invalidity because patentee did not meet burden of production that claims were entitled to priority date). First, his testimony has no weight on the (b)(2)(C) exception, as he never testified that he (1) spoke to anyone at UTC regarding patent ownership; (2) reviewed any documents other than the Orange Book; or (3) had any basis for knowing whether the patents were assigned to UTC prior to April 17, 2020. *See EcoFactor, Inc. v. Google LLC*, 137 F.4th 1333, 1344 (Fed. Cir. 2025) (holding that executive's testimony that "referenced no evidentiary support" was "an unsupported assertion from an interested party" that "cannot provide a sufficient factual basis"); *Acceleration Bay LLC v. Activision Blizzard Inc.*, 2018 WL 5045186, at *1-2 (D. Del. Oct. 17, 2018) (precluding testimony from lay witness where he had "no independent knowledge" of proffered facts). In fact, Dr. Bryd's testimony was based on a demonstrative of the Orange Book listing for Tyvaso, consistent with his limited knowledge of "ownership." Tr. 35:17-36:24 (testifying about PDX2, 3). Second, UTC would have the Court construe Dr. Byrd's testimony as to when the "issued patents" were "first filed" as evidence of UTC's undivided ownership of both patents as of April 17, 2020—but that is not his testimony. Tr. 36:22-24. Issued patents are not "filed" with the PTO, but they are "filed" for listing in the Orange Book. Given Dr. Byrd's admittedly limited knowledge based on the Orange Book and the question he was asked, the testimony can only be interpreted to mean that UTC owned the '793 and '327 patents "listed on the slide," from the time they were "first filed" in the Orange Book. Tr. 36:13-24. Third, Dr. Byrd did not testify as to any specific date that any particular patent was "first filed" with either the FDA or the PTO. Tr. 35:14-36:24. Nonetheless, no "patent" can be "filed" with FDA until it issues, which occurred after April 2020.

Fourth, Dr. Byrd's testimony critically failed to establish UTC owned ***all*** of the rights to any patent, and the timing of any conveyance of ownership rights to UTC. *Id.*; FOF14; MPEP

717.02(a)[2] (to invoke the (b)(2)(C) exception, the patent owner must show that "the person(s) or organization(s)/business entity(ies) own 100 percent of the subject matter and 100 percent of the claimed invention.").

Finally, even assuming Dr. Byrd's testimony related to PTO filings (and not Orange Book filings), his testimony relates to ownership as of April 16, 2021—the filing date of the *non-provisional* application that led to the '327 patent, April 16, 2021—a year after the April 17, 2020 filing date of the '810 provisional application. JTX1 ("Related U.S. Appl. Data"); Tr. 36:22-24. Dr. Byrd was never asked about ownership as of the '810 provisional application's filing date. Nor was he asked about ownership as of any "issued patent['s]" *effective* filing date. He was only asked about ownership as of "issued patents" being "first filed." Thus, even if the filing he was referencing was the filing that led to the issuance of the patent, "issued patents" would have been "first filed" on the date for the non-provisional applications. As the Federal Circuit has stated, provisional applications are "a temporary, stand-in application that precedes the non-provisional application and does not lead to a conferral of rights on the patentee unless a patent issues from the subsequent non-provisional application." *In re Forest*, 134 F.4th 1198, 1203 (Fed. Cir. 2025).

Moreover, Dr. Byrd's conclusory testimony fails to meet UTC's burden of production for the (b)(2)(C) exception. In the sole case UTC relies on for the exception, Pfizer did not meet its burden simply being named as assignee on the prior art and the challenged patent. *See Sanofi Pasteur Inc. v. Pfizer Inc.*, IPR2018-00188, Paper 10 at 13-14 (PTAB June 5, 2018) (referencing Ex. 1009 and Ex. 1010 (prior art) and Ex. 1001 (challenged patent)). Rather, Pfizer provided

[2] "The MPEP is commonly relied upon as a guide to patent attorneys and patent examiners on procedural matters. Although the MPEP does not have the force of law, it is entitled to judicial notice so far as it is an official interpretation of statutes or regulations with which it is not in conflict." *Airbus SAS v. Firepass Corp.*, 793 F.3d 1376, 1380 (Fed. Cir. 2015) (citation modified).

documentary evidence of ownership, including assignment agreements and patent office assignment records, establishing that the challenged patent ***and*** prior art patents were fully commonly owned as of the effective filing date of the challenged patent. *Id*. at 13-14; *see also US Conec Ltd. v. Senko Advanced Components, Inc.*, IPR2024-00119, Paper 9 at 34-38 (PTAB July 9, 2024) (finding (b)(2)(C) exception applied when patent owner submitted executed assignments, proof of assignment recordation with PTO, and agreements evidencing obligation to assign patent rights). No such documentation is in evidence here.

UTC made the strategic decision to rely only on a single question to Dr. Byrd to address patent ownership even though it had unique control over documents and testimony relevant to the (b)(2)(C) exception. Two inventors testified—Dr. Smith[3] (both live and via deposition) and Dr. Deng (via deposition)—yet neither provided testimony about any alleged assignments to UTC. FOF13, 15. The third inventor, Dr. Peterson, was listed on UTC's witness list but not called. *Id.* Stephen Maebius, UTC's patent prosecution counsel, testified via deposition, but provided no testimony on any alleged assignments. FOF16. Tellingly, the person most uniquely qualified to testify about UTC's alleged patent assignments, Mr. Shaun Snader, UTC's VP and associate general counsel of intellectual property, sat at counsel table every day of trial and briefly testified via deposition, but he never spoke on the (b)(2)(C) exception. FOF16. Moreover, UTC failed to offer any documentary evidence regarding patent assignments, employment agreements, or any other materials evidencing any ownership rights in either patent into evidence. Notably, UTC did not put any assignment or employment related material on its exhibit list. *See* D.I. 362, 10.

[3] Dr. Smith testified live immediately after UTC made its oral 52(c) motion. Tr. 684:8-686:16 (Rule 52(c) motions); 686:17-699:6 (Smith live testimony).

UTC's argument in the Rule 52(c) motion that Liquidia cannot dispute common ownership of the '793 and '327 patents is meritless. UTC cites invalidity contentions that are not in the record, and those contentions merely acknowledge that the '327 and '793 patents are currently owned by UTC, and say nothing of the timing of that ownership in relation to the effective filing date, the essential fact for UTC's (b)(2)(C) challenge. D.I. 398, 8.

Liquidia has met its burden of proof that the '793 patent is prior art and UTC failed to meet its burden of production that the (b)(2)(C) exception applies. Accordingly, the '793 patent is prior art to the '327 patent.

2. The '793 Patent and Its Disclosure Is Applicant Admitted Prior Art

Regardless of the §102(b)(2)(C) exception, the '793 patent and its disclosure also qualify as applicant admitted prior art ("AAPA"). The Federal Circuit is clear that "admissions in the specification regarding the prior art are binding on the patentee for purposes of a later inquiry into obviousness." *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1362 (Fed. Cir. 2007); *see also Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1570 (Fed. Cir. 1988) ("A statement in the patent that something is in the prior art is binding on the applicant and patentee for determinations of anticipation and obviousness."); *Sjolund v. Musland*, 847 F.2d 1573, 1577-79 (Fed. Cir. 1988); *Qualcomm Inc. v. Apple Inc.*, 24 F.4th 1367, 1375 n.11 (Fed. Cir. 2022) ("As recognized in *PharmaStem*, our precedent treats AAPA as binding on the patentee") (citation omitted). An express statement that admitted subject matter is "prior art" is not required, as *PharmaStem* held statements in the specification that subject matter was previously "shown" or "demonstrated" qualified as applicant admitted prior art. *PharmaStem*, 491 F.3d at 1361-62.

The inventors admitted in the '327 specification that "[p]ulsed inhalation devices are disclosed, for example, in . . . U.S. Patent No[]. . . . 10,716,793." FOF17; JTX1, 20:48-57. Dr. Nathan confirmed this admission, as he testified that the '327 patent incorporated the '793 patent's

description of dry powder inhalers and dry powder compositions of treprostinil. FOF17; Tr. 897:6-898:5. Until the trial, UTC repeatedly told the Court that the '793 patent was prior art to the '327 patent. During the PI hearing, UTC's lead counsel confirmed that "the disclosure of the '793 patent is prior art." 2024-04-23 PI Hearing Tr. 22:16-19 ("THE COURT: Well, so do you agree that the -- I believe its the '793 patent, but is prior art?" A. MR. CARSTEN: Certainly, the disclosure of the '793 patent is prior art.")[4] This is a binding judicial admission. *See Bedrosian v. United States Dep't of Treasury, IRS*, 42 F.4th 174, 184-85 (3d Cir. 2022) (finding counsel's opening statements qualified as a judicial admission). In the PI briefing, UTC admitted that the '793 patent was considered by the examiner during prosecution as part of a "prior art search" conducted by the PTO. FOF18 ("there can be no dispute that the '793 patent . . . was before the examiner during prosecution" and Dr. Nathan stating under oath "On August 21, 2022 a prior art search was performed by the USPTO" and returned results "including the '793 patent."). Dr. Nathan testified in response to inequitable conduct allegations that materials UTC withheld from the examiner were "cumulative" to the '793 patent. FOF18. Cumulativeness is irrelevant if the '793 patent is not prior art. *See also* D.I. 239, 3-4 (UTC asserting information is cumulative to the '793 patent, not that the '793 patent lacks prior art status).

The admissions that the '793 patent and its disclosure are prior art bind UTC even if the prior art would not otherwise qualify under §102. In *Nomiya*, the court held that admitted prior art in a patent application that did not otherwise qualify as prior art under §102 was still a binding admission "considered 'prior art' for any purpose, including use as evidence of obviousness under § 103." *In re Nomiya*, 509 F.2d 566, 570-71 & n.5 (CCPA 1975) (admission that certain matter is

[4] Mr. Carsten noted that "[t]here may be some technical argument as to why the *claims* of the '793 patent as issued are not" prior art (*id.* (emphasis added)), but even if true, the admitted prior art *disclosure* of the '793 patent still invalidates as discussed below. *See infra* IV.B-G.

"prior art" is binding for "*all* purposes, whether or not a basis in § 102 can be found for its use as prior art") (emphasis added). Similarly, in *Tyler Refrigeration v. Kysor Indus. Corp.* the court affirmed the district court's decision that an admission that a patent was prior art, even though it did not otherwise qualify under §102, rendered the patent prior art and was binding. 777 F.2d 687, 690 (Fed. Cir. 1985); *see also Tyler Refrigeration Corp. v. Kysor Indus. Corp.*, 601 F. Supp. 590, 600-01 (D. Del. 1985) (providing additional facts related to the Federal Circuit's decision).

Because the '327 patent inventors admit the '793 patent is prior art, confirmed by UTC's counsel and expert, the '793 patent is AAPA to the '327 patent and not subject to any exception.

B. Claim 1 Is Obvious

1. *Faria-Urbina* Discloses the Limitations of Claim 1

Faria-Urbina, authored by Dr. Waxman and published in 2018, is a study of 22 Group 3 PH patients, including 14 PH-ILD patients, treated with Tyvaso and followed for at least three months. FOF19-21. *Faria-Urbina* reports Tyvaso administration led to improvements in exercise capacity, specifically improvements in 6MWD, in the PH-ILD patients. FOF24-26. The patients received Tyvaso four times daily using dosing that began at three breaths (6 mcgs/breath) and increased to a maximum of 9 to 12 breaths (at least 54 mcgs) per session, which, Drs. Channick and Nathan confirmed, a POSA understands falls within the claimed effective dosing. FOF25-26. *Faria-Urbina* discloses all the limitations of claim 1 and renders claim 1 obvious. FOF21-27.

Dr. Nathan's claim that *Faria-Urbina* is "garbage" that no rational POSA would rely on is not credible because (i) it reports real-world treatment of patients, and (ii) Dr. Waxman's work was the rationale and motivation to perform INCREASE. FOF21, 27, 48-57. Dr. Nathan's suggestion that the patients in *Faria-Urbina* had PAH rather than PH-ILD, including because they had "severe" PH, is also not credible because these patients have the same PH severity as patients in INCREASE, and fall within the PH-ILD criteria that Dr. Nathan published. FOF2, 3, 6, 22, 23.

Dr. Waxman had access to the patients and diagnosed PH-ILD with the same right heart catheterization ("RHC") and high-resolution computed tomography ("HRCT") that Dr. Nathan said were required. FOF1, 22-23. The Court should reject Dr. Nathan's second-guessing without access to the patients or the diagnostic tests he said was critical for diagnosis.

2. The '793 Patent Discloses the Limitations of Claim 1

The '793 patent discloses methods of treating patients with PH, including PH-ILD, using iTre. FOF28-31. This Court has already determined that the '793 patent encompasses all five WHO PH Groups, including PH-ILD. FOF30. UTC also admitted to the USPTO and FDA the '793 patent covers the Tyvaso PH-ILD indication–improving exercise capacity. FOF31. The '793 patent describes administering treprostinil "by inhalation," satisfying the claimed route of administration. FOF30-32, 69. It also discloses the use of an inhaler to administer about 15 to 100 mcgs of treprostinil in a single event, which a POSA would understand overlaps the claimed dosing of the '327 patent. DTX2, 20; FOF32-33.

3. A POSA Would Be Motivated to Combine *Faria-Urbina* and the '793 Patent with a Reasonable Expectation of Success

"The standard to find a motivation to combine is far below what is sufficient to prove safety and efficacy to the FDA." *Persion Pharms. LLC v. Alvogen Malta Operations Ltd.*, 945 F.3d 1184, 1192 (Fed. Cir. 2019) (citation omitted). Here, a POSA would have been motivated to combine *Faria-Urbina* and the '793 patent because they are directed to the same subject matter—use of the same drug (treprostinil), delivered via the same route (inhaled), with the same dosing, to treat PH-ILD patients. FOF34-35. A POSA's motivation is not a hypothetical inquiry in this case because *Faria-Urbina*, as well as other prior art and testimony of multiple doctors, proves that POSAs were actually motivated to use Tyvaso off-label at the claimed dosing in PH-ILD patients and achieved actual success in improving exercise capacity. FOF36-58.

The law is clear that a POSA need not predict success with absolute certainty, nor must the prior art demonstrate conclusive clinical efficacy. *See, e.g.*, *Eli Lilly & Co. v. Teva Pharms. Int'l GmbH*, 8 F.4th 1331, 1346 (Fed. Cir. 2021) ("[A] showing of a reasonable expectation of success in a method of treatment claim need not rely on clinical data … nor must it include a demonstration of certainty that the treatment would be successful in every instance."). Each of *Faria-Urbina* and the '793 patent independently provide more than a reasonable expectation of success. FOF34-35. *Faria-Urbina* reports actual improvements in exercise capacity after administration of Tyvaso in one or more patients at the claimed dosing, and UTC admitted that the '793 patent covers Tyvaso's approved indication of improving exercise capacity in PH-ILD patients. FOF24-26, 30-32.

Dr. Nathan's opinion that a POSA would require a randomized placebo-controlled trial and nothing short of the actual results of INCREASE to have a reasonable expectation of success is contrary to law. FOF66. *Acorda Therapeutics, Inc. v. Roxane Lab'ys, Inc.*, 903 F.3d 1310, 1333-34 (Fed. Cir. 2018) (finding that a POSA "*can* draw reasonable inferences about the likelihood of success even without a perfectly designed clinical trial showing a statistically significant difference in efficacy between a specific dose and placebo").

A decade of successful off-label treatment corroborated by prior art publications and presentations, admissions in UTC's own documents, and admissions by its CEO, Dr. Rothblatt, conclusively establish a motivation to combine with a reasonable expectation of success. FOF36-58. Soon after Tyvaso's approval in 2009 for PAH, doctors around the country were treating PH-ILD patients off-label with Tyvaso and observing improvements in exercise capacity. FOF36, 117-122. This successful off-label use is corroborated by contemporaneous reports in prior art publications and presentations, including *Agarwal*, Dr. Waxman's 2017 John Vane Memorial Symposium presentation, and *Parikh*. FOF38-47, 57. *Agarwal,* a publicly presented 2015 abstract

authored by Dr. Waxman, reports significant improvements in exercise capacity in PH-ILD patients, who were treated with Tyvaso using the claimed dosing. FOF39-40. Dr. Waxman used this successful off-label treatment of PH-ILD with Tyvaso, to convince UTC to conduct INCREASE. FOF41, 48-55. In 2017, Dr. Waxman publicly presented his successful off-label treatment and provided the rationale for using iTre to treat PH-ILD patients, leading to *Faria-Urbina*. FOF46-47. *Parikh*, a 2016 peer-reviewed publication authored by Dr. Tapson, details successful off-label Tyvaso use at the claimed dosing in PH-ILD patients. FOF42-45. *Parikh* reports improvements in exercise capacity (6MWD) and NT-proBNP. FOF45.

Multiple UTC documents confirm that Dr. Waxman's work in *Agarwal* and *Faria-Urbina*, rather than any conception by UTC or the named inventors, was the rationale and proof of concept that formed the basis for conducting INCREASE with at least a reasonable expectation of success. FOF48-58. In a 2018 Earnings Call, Dr. Rothblatt publicly confirmed that doctors—including Dr. Waxman—had been treating PH-ILD patients off-label with Tyvaso, were observing improvements in exercise ability, and presented these findings in publications and presentations, which she confirmed permitted UTC to "power" INCREASE. DTX3, 10; FOF57. Dr. Waxman's and others' decade-long successful off-label use of Tyvaso in PH-ILD proves that the '327 patent was obvious to POSAs even if Dr. Nathan claims it was not obvious to UTC. FOF36-37, 119-122; *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 420 (2007) ("The question is not whether the combination was obvious to the patentee, but whether the combination was obvious to a [POSA]."). The evidence establishes a motivation, with a reasonable expectation of success, in achieving claim 1 of the '327 patent based on *Faria-Urbina*, the '793 patent, or their combination.

Dr. Nathan relied on allegedly "failed" studies to argue a POSA would not have a reasonable expectation of success. These studies are irrelevant because they involve different

drugs, different dosing, and different routes of administration compared to the closest prior art. FOF59, 61. Their irrelevance is proven by doctors' continued off-label use of Tyvaso in PH-ILD patients even with the knowledge of these studies. FOF60-64, 117-122. Further, Dr. Nathan's reliance on the "failed" studies is not credible as it directly contradicts his rationale that a POSA would not rely on *Saggar 2014* because it is "a different formulation of a drug given in a different way." FOF65, 82. Accordingly, claim 1 is obvious.

C. Claim 17 Is Obvious

Claim 17 requires an increase in 6MWD "by at least 10 m after 8 weeks of administering" inhaled treprostinil. JTX1, 51; FOF67. Tables S3 and S4 of *Faria-Urbina* report increases in 6MWD of 21 and 55 meters respectively in PH-ILD patients, meeting claim 17. FOF24, 67. These patients were followed "for at least 3 months," which is after 8 weeks as required. FOF25, 67. Claim 17 is obvious over *Faria-Urbina*, as a POSA would be motivated with a reasonable expectation of success for the same reasons discussed for claim 1. *See supra* § IV.B.3; FOF67.

D. Claim 14 Is Obvious

Claim 14, which depends from claim 11, requires the inhaled administration of claim 1 to be performed with a pulsed inhalation device and that said device is a "dry powder inhaler." JTX1, 50; FOF68. In addition to PH-ILD, the '793 patent specification describes inhaled dry powder formulations of treprostinil and DPIs for their delivery. FOF69. Claim 14 is obvious from this disclosure and its combination with *Faria-Urbina*.

Additionally, as acknowledged by Dr. Nathan, the '327 patent incorporates by reference other prior art, including WO2019/237028, the '507 patent, ***and*** the '793 patent for their disclosures of making and using treprostinil dry powder formulations and DPIs. FOF70. The '507 patent, which issued on May 17, 2016, is in the same family as the '793 patent and shares the same specification. FOF70. UTC's counsel also previously admitted that WO2019/237028 (Guarneri)

is prior art to the '327 patent. D.I. 123, 42-43 (pointing to Guarneri); Markman Tr. (D.I. 153), 38:11-18. UTC's counsel also previously admitted in this case that the disclosure of the '793 patent (which is the same as the '507 patent and the only portion of the '793 patent upon which Liquidia relies) is prior art. 2024-04-23 PI Hearing Tr. 22:16-19. These prior art disclosures of making treprostinil dry powders with DPIs, incorporated in the '327 patent, further render claim 14 obvious in combination with *Faria-Urbina*. FOF70-71; *PharmaStem*, 491 F.3d at 1362; *Constant*, 848 F.2d at 1570 ("A statement in the patent that something is in the prior art is binding on the applicant and patentee for determinations of anticipation and obviousness.").

Dr. Nathan separately asserted that a POSA would not be able to formulate a dry powder formulation of treprostinil with a suitable DPI. FOF8; Tr. 865:9-23, 894:8-895:17. But DPIs were well known to POSAs for delivering inhaled medications, including treprostinil dry powders, and this knowledge must be considered for obviousness independent of the '793 patent. FOF70-73; *Randall Mfg. v. Rea*, 733 F.3d 1355, 1362 (Fed. Cir. 2013) ("[T]he knowledge of such an artisan is part of the store of public knowledge that must be consulted when considering whether a claimed invention would have been obvious."). UTC admitted in the prior case before this Court that by 2006, it was well-known how to develop dry powder formulations of treprostinil—including identifying suitable DPIs. FOF71-72.[5] This Court agreed with UTC, and was affirmed. *See UTC v. Liquidia*, 624 F. Supp. 3d 436 (D. Del. 2022), *aff'd*, 74 F.4th 1360 (Fed. Cir. 2023); FOF72. UTC's prior admissions, adopted by the Court, further establish that claim 14 is obvious.

And UTC is collaterally estopped from arguing that dry powder formulations of treprostinil with a suitable DPI were not obvious as of 2006 because (1) the identical issue regarding the

[5] This Court may take judicial notice of UTC's Proposed Findings of Fact on Invalidity and the Court's trial opinion from the previous action between the parties. *See Purdue Pharma L.P. v. Accord Healthcare Inc.*, 2023 WL 5835811, at *2 (D. Del. Sept. 8, 2023) (citation omitted).

availability of dry powder formulations of treprostinil and DPIs as of 2006 was actually litigated by the parties before this court; (2) this court's determination was necessary for its ruling that dry powder formulations of treprostinil were enabled as of 2006; and (3) UTC's interests were fully represented in the previous trial. FOF71-73; *see also Purdue Pharma L.P. v. Accord Healthcare Inc.*, 2024 WL 4120717, at *21 (D. Del. Sept. 9, 2024) (explaining that collateral estoppel would bar plaintiff from asserting an argument contrary to the court's previous findings regarding the same issue); *Franklin Sav. Corp. v. United States*, 56 Fed. Cl. 720, 736 (Fed. Cl. 2003) ("*Collateral estoppel* applies equally to findings of fact and conclusions of law.").

A POSA would also be motivated with a reasonable expectation of success to replace the nebulized formulation of *Faria-Urbina* with a more convenient DPI. FOF74-75. Further, because both devices deliver treprostinil through the same locally acting inhaled route, a POSA would expect them to achieve the same therapeutic effect, confirming a reasonable expectation of success. FOF76. For these reasons, claim 14 is obvious.

E. Claim 5 Is Obvious

Claim 5 depends from claim 1 and requires a reduction of "plasma concentration of NT-proBNP in the [PH-ILD] patient by at least 200 pg/ml after 8 weeks, 12 weeks, or 16 weeks." JTX1, 50; FOF90. *Saggar 2014* discloses this limitation, and a POSA would have been motivated with a reasonable expectation of success combining it with *Faria-Urbina* and/or the '793 patent. FOF77, 90-92.

1. Saggar 2014

Saggar 2014 is a peer-reviewed publication, authored by Dr. Rajan Saggar in 2014, reporting improvements in hemodynamics, exercise capacity, BNP levels, and FVC in PH-ILD patients following IV treprostinil administration (Remodulin). FOF78-81. Patients treated with treprostinil experienced a statistically significant reduction in BNP levels from 558 pg/ml to 228

pg/ml—a difference of 330 pg/ml, after 12 weeks, with a p-value of 0.004. FOF91; DTX10, 5 (Table 4). According to the unrebutted testimony of Drs. Channick and Saggar, BNP and NT-proBNP (a fragment of BNP) are both cardiac function biomarkers in PH and are positively correlated. FOF91-92. There is no clear advantage in using one biomarker over the other and a POSA would have understood that *Saggar 2014*'s statistically significant reduction of BNP levels would correlate with a similar magnitude of reduction in NT-proBNP. *Id*. *Parikh* confirmed this positive correlation between BNP and NT-proBNP, reporting decreased NT-proBNP after iTre administration in Group 3 PH patients, including PH-ILD patients. FOF91. A POSA would therefore believe *Saggar 2014*'s disclosure of reduced BNP levels correlates to a corresponding decrease in NT-proBNP levels of at least 200 pg/ml after 8, 12, or 16 weeks. FOF90-92.

2. A POSA Would Be Motivated to Combine with Reasonable Expectation of Success

A POSA would be motivated with a reasonable expectation of success because despite the IV administration of treprostinil in *Saggar 2014*, all three references disclose using treprostinil in the same patient population, and report similar results for hemodynamics and improvements in exercise capacity. FOF83, 88-89; DTX348, 1; DTX10, 1; DTX2, 1. This is expected because whether administered systemically or inhaled locally, treprostinil still works as a prostacyclin vasodilator in PH-ILD patients. FOF83, 87. It is not a legal requirement that *Saggar 2014* disclose inhaled administration, because a POSA would recognize that the results from *Saggar 2014* are applicable to the inhaled route disclosed in both *Faria-Urbina* and the '793 patent. *Belden Techs. Inc. v. Superior Essex Commc'ns LP*, 802 F. Supp. 2d 555, 563, 573 (D. Del. 2011).

A POSA would also be motivated with a reasonable expectation of success to replace the IV administration of treprostinil in *Saggar 2014* with the inhaled route for its obvious convenience benefits and to minimize the chances of V/Q mismatch. FOF83-87. In fact, *Faria-Urbina* cites

Saggar 2014 as motivation to treat PH-ILD patients with iTre. FOF84. Accordingly, a POSA would have a reasonable expectation of achieving the claimed reduction in NT-proBNP based on the disclosures of *Saggar 2014* and *Parikh* because of the unrebutted correlation between BNP and NT-proBNP and the demonstration of reduction in NT-proBNP in *Parikh*. FOF90-92.

F. Claim 6 Is Obvious

Claim 6 depends from claim 1 and requires "a statistically significant reduction of at least one exacerbation[] of the [ILD]." JTX1, 50; FOF93. Patients experiencing exacerbations present with symptoms including shortness of breath ("dyspnea"), respiratory distress resulting in reduced oxygen levels, and/or declining functional class. FOF94.

The PH-ILD patients treated with iTre in *Faria-Urbina* experienced the opposite of what would be expected for patients experiencing exacerbations, namely these patients got better and exhibited a decrease in dyspnea, statistically significant improvements in 6MWD (*i.e.*, reductions in respiratory deterioration), and significant improvements in functional class. FOF95; DTX348, 1, 5 (Table 2). The patients in *Saggar 2014* also had statistically significant improvements in 6MWD and decreased dyspnea. DTX10, 3-4; FOF96. A POSA would understand the statistically significant improvements in exercise capacity and functional class correspond to reduced exacerbations. FOF94-98. Further, these improvements indicate to a POSA that the patients in *Faria-Urbina* and *Saggar 2014* are getting better, not worse, and would therefore provide a POSA with a reasonable expectation of success in achieving a statistically significant reduction in an exacerbation of lung disease if performed using iTre in a larger patient population. FOF97-98.

G. Claim 9 Is Obvious

Claim 9 depends from claim 1 and requires a "statistically significant improve[ment] of [FVC] in the [PH-ILD] patient" after 8, 12, or 16 weeks. JTX1, 50; FOF99-100. *Saggar 2014* reports an improvement of 1% in terms of predicted FVC in the treated patient population, as

shown in Table 2, reporting a change in percent predicted FVC from 62% at baseline to 63% at 12 weeks. FOF101-102. The 1% improvement in FVC in *Saggar 2014* is the same change in percent predicted FVC observed in INCREASE and reported in the '327 patent (0.77% and 1.07% at weeks 8 and 16, respectively), which corresponded to a statistically significant improvement in percent predicted FVC. FOF102-104. Moreover, the improvement response rate in FVC in *Saggar 2014* is also comparable to INCREASE. FOF104. Because the magnitude and response rate of FVC improvement in *Saggar 2014* correspond to a statistically significant improvement of FVC in INCREASE, a POSA would understand that *Saggar 2014* discloses and provides a reasonable expectation of successfully achieving the claimed statistically significant improvement in FVC. FOF103-104. Dr. Saggar confirmed that no later than 2010, he developed the expectation that treprostinil would improve FVC in PH-ILD patients in the same way that it improves FVC in some PAH patients. FOF101. A POSA would also be motivated with a reasonable expectation of success to achieve the same results using iTre for these reasons and those discussed for claim 5. *See supra* § IV.E.

H. UTC's Secondary Considerations Do Not Establish Non-Obviousness

UTC produced no persuasive evidence of secondary considerations that can overcome the strong showing of obviousness. *See, e.g.*, *Ohio Willow Wood Co. v. Alps S., LLC*, 735 F.3d 1333, 1344 (Fed. Cir. 2013). **No Nexus:** UTC failed to show that any objective indicia have a nexus to purportedly nonobvious aspects as opposed to the known efficacy of iTre in PH-ILD patients. *See In re Huai-Hung Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011); *see also In re Huang*, 100 F.3d 135, 140 (Fed. Cir. 1996). In fact, Dr. Nathan never compared the claims of the '327 patent to the closest prior art as required. FOF105-107; *see Adapt Pharma Operations Ltd. v. Teva Pharms. USA, Inc.*, 25 F.4th 1354, 1373 (Fed. Cir. 2022). UTC admitted the '793 patent claims the same indication and dosing as the '327 patent (FOF31-32), and failed to provide any evidence of a

material difference attributable to the '327 patent. FOF106. **No Unexpected Results**: UTC's unexpected results rely on the allegedly "failed" studies, which are irrelevant and do not support that the results of either INCREASE or the claims are unexpected for the same reasons discussed above. *See supra* § IV.B.3. Additionally, Dr. Nathan's arguments are legally insufficient to support unexpected results because he does not compare the patent to the closest prior art (*e.g.*, *Faria-Urbina*). FOF107-108. **No Evidence of Skepticism:** Corroborated testimony of multiple POSAs confirms that they continued using inhaled treprostinil to improve the exercise capacity in their PH-ILD patients despite the "failed" studies, making clear that Dr. Nathan's skepticism was based on his own subjective beliefs—not that of the industry. FOF109-111; *see Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 923 F. Supp. 2d 602, 680 (D. Del. 2013). **No Long-Felt but Unmet Need:** UTC cannot establish this factor with respect to the '327 patent because it already admitted that the need was met by the '793 patent. FOF112. **No Copying:** Dr. Nathan's testimony ignores that Yutrepia is a different drug than Tyvaso, as it has an entirely different formulation and is delivered via dry powder as opposed to a nebulizer. FOF116. He also ignores that Liquidia amended its label to include PH-ILD before the '327 patent claims issued. FOF116. Dr. Nathan's testimony falls well short of establishing copying. Dr. Nathan's testimony on **Teaching Away**, **Industry Praise**, and "**Success**" is facially insufficient. FOF113-115. UTC has, therefore failed to prove the existence of any secondary consideration.

V. CLAIMS 1, 5, 6, 9, AND 17 ARE INVALID DUE TO PRIOR SALE

A patent claim is invalid under the on-sale bar if the invention was on sale before the effective filing date. *See* 35 U.S.C. §102(a)(1). The on-sale bar applies if, before the effective filing date, the claimed invention was both (1) the subject of a commercial offer for sale and (2) ready for patenting. *See Helsinn Healthcare S.A. v. Teva Pharms. USA, Inc.*, 586 U.S. 123, 130-31 (2019). As discussed below, both prongs are met here with respect to claims 1, 5, 6, 9, and 17.

A. Tyvaso Was Commercially Sold to Improve Exercise Capacity in PH-ILD Patients Prior to April 2019

A claimed invention is "the subject of a commercial offer for sale" if there is a commercial offer for sale and the offer is for the patented invention. *See Scaltech, Inc. v. Retec/Tetra, LLC*, 269 F.3d 1321, 1328 (Fed. Cir. 2001). A claimed process is "on-sale" even if the seller did not recognize that it possessed the features later claimed. *Id.* at 1330-31. The on-sale bar applies so long as the item offered for sale embodied the claimed invention, regardless of whether the parties to the transaction recognized that fact at the time. *Abbott Lab'ys v. Geneva Pharms., Inc.*, 182 F.3d 1315, 1319 (Fed. Cir. 1999).

1. Doctors Treated PH-ILD Patients with Tyvaso and Saw Improvements in Their Exercise Capacity Prior to April 2019

Tyvaso was approved by the FDA for the treatment of PAH in 2009. FOF117. UTC also began selling Tyvaso in 2009 along with prescribing information. FOF123; DTX357, 2.

Shortly after Tyvaso was approved in 2009, Drs. Hill, Waxman, Tapson, Saggar, and Channick independently began to prescribe Tyvaso off-label to treat PH-ILD patients. FOF119-122. The doctors prescribed Tyvaso using the same dosing—3 breaths of Tyvaso four times daily, titrating up to 9-12 breaths four times daily, with each breath containing 6 mcg of treprostinil. FOF122. This dosing is consistent with that in claim 1 of the '327 patent, the 2009 Tyvaso label, the 2021 Tyvaso label, and that used in the INCREASE study. FOF122. The doctors saw their patients improve in exercise capacity, including in 6MWD. FOF120. Dr. Saggar also observed reductions in NT-proBNP levels. FOF120.

Each doctor was qualified to diagnose PH-ILD. FOF121. Notably, Drs. Waxman and Tapson were on the steering committee of INCREASE, and Dr. Hill was an investigator in INCREASE, evidencing their ability to accurately diagnose PH-ILD. FOF121.

The doctors' real-world treatment of PH-ILD patients with Tyvaso is corroborated by

multiple publications. *Faria-Urbina* corroborates Dr. Waxman's treatment of PH-ILD and CPFE patients using Tyvaso with standard dosing and further reports improvements in exercise capacity, including 6MWD. FOF129. *Parikh* corroborates Dr. Tapson's use of Tyvaso with the same dosing and reports improvements in both 6MWD and NT-proBNP. FOF129. Both publications were peer-reviewed and the treatments described therein were not part of a clinical trial. FOF129. UTC's 2018 Earnings Call further confirmed that doctors enabled their PH-ILD patients to benefit from Tyvaso. FOF127, 57. This consistent and widespread off-label use—which started well before April 2019—demonstrates that Tyvaso was being used to treat PH-ILD patients in a manner that satisfies the claimed limitations. FOF119-122.

2. Tyvaso Was Prescribed and Sold to PH-ILD Patients to Improve Their Exercise Capacity Prior to April 2019

The claimed invention of the '327 patent was on sale under §102(a) because Tyvaso was the subject of a sale to PH-ILD patients. In treating their PH-ILD patients with Tyvaso, Drs. Hill, Waxman, Tapson, Saggar, and Channick secured insurance coverage for the Tyvaso prescriptions. FOF124-127. As Dr. Hill explained, doctors routinely submitted forms to insurers indicating the patient had PH-ILD. FOF124. Insurers would sometimes deny coverage, but doctors quickly learned how to secure approval. FOF124-126. The fact that insurers denied coverage establishes that the prescriptions were not for PAH—otherwise they would have been approved. FOF125. Further, the fact that doctors ultimately secured insurance coverage is direct evidence that there was a commercial sale of Tyvaso for PH-ILD patients.

These sales were corroborated by UTC's CEO during the 2018 Earnings Call, where she stated that "through the kindness and generosity of certain payers around the country who have gone ahead and upon the initiative of their doctors, were able to enable some WHO Group III patients to benefit" from Tyvaso, including patients with PH-ILD. DTX3, 10; FOF127. She also

confirmed that patients saw improvements in their exercise capacity. *Id.* This admission is more evidence of the sale of Tyvaso to PH-ILD patients for the purpose of improving exercise capacity.

The doctors' treatment of their PH-ILD patients with Tyvaso was not experimental, it was not part of a clinical trial, nor were the patients receiving Tyvaso for free. FOF128. Nonetheless, experimental use applies only to the actions of the inventors and their agents, not of third parties. *See Atlanta Attachment Co. v. Leggett & Platt, Inc.*, 516 F.3d 1361, 1366 (Fed. Cir. 2008).

UTC also argues that the claimed invention was not on sale because the Tyvaso prescribed by the doctors was for PAH, not PH-ILD, patients. But each doctor was qualified to accurately diagnose PH-ILD (FOF121), and it is unrefuted that Drs. Hill and Saggar experienced denials from insurers, then eventual approval to cover Tyvaso for PH-ILD. FOF124-126. Indeed, there would have been no justification for insurance companies to deny coverage if the patient were diagnosed with pure PAH instead of PH-ILD. FOF125. And finally, sales to PH-ILD patients were confirmed by Dr. Rothblatt. FOF127.

UTC's argument that there can be no prior sale within the meaning of §102(a) because any sale was made by specialty pharmacies, not UTC, and was not publicly disclosed is legally incorrect. Section 102(a) is not limited to commercial sales by the inventor—it also applies to commercial sales made by intermediaries like specialty pharmacies. *See Special Devices, Inc. v. OEA, Inc.*, 270 F.3d 1353, 1355 (Fed. Cir. 2001) ("By phrasing the statutory bar in the passive voice, Congress indicated that it does not matter who places the invention 'on sale'; it only matters that someone—inventor, supplier or other third party—placed it on sale."); *see also In re Epstein*, 32 F.3d 1559, 1564 (Fed. Cir. 1994). And here, UTC knew Tyvaso was being sold to PH-ILD patients, and made no effort to stop it; instead Dr. Rothblatt applauded the fact that PH-ILD patients had access to Tyvaso and it was covered by insurance. FOF127. Finally, these sales

were not secret, as evidenced by Dr. Rothblatt's 2018 statements. *Id*. Regardless, even secret sales are still invalidating. *See Helsinn*, 586 U.S. at 131.

That the '327 patent claims a method does not prohibit application of the on-sale bar. A method claim may be "on-sale" where a product is sold and used to perform the claimed method. *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 424 F.3d 1276, 1285-86 (Fed. Cir. 2005) (invalidating method claim directed to performing a hybridization assay based on the sale of a nucleic acid probe); *Petrolite Corp. v. Baker Hughes Inc.*, 96 F.3d 1423, 1426-27 (Fed. Cir. 1996) (affirming invalidity of a method claim based on sale of compound used to practice claimed method). Here, the sale of Tyvaso to PH-ILD patients, who used Tyvaso to obtain therapeutic benefits including improvements in exercise capacity, satisfies the on-sale bar because Tyvaso embodies the essential feature of the '327 patent claims. Because the prescriptions identified the patients as having PH-ILD, the sales were specifically for the treatment of PH-ILD. FOF124-126; Tr. 600:17-606:1.

B. Claims 1, 5, 6, 9, and 17 Were Ready for Patenting Prior to April 2019

An invention is ready for patenting when it has either been (1) reduced to practice or (2) sufficiently disclosed such that a person of ordinary skill in the art would be able to practice the invention. *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 67-68 (1998); *Helsinn*, 586 U.S. at 130.

1. Claim 1 Was Reduced to Practice Prior to April 2019

Reduction to practice requires (1) possession of the invention and (2) it was shown to work for its intended purpose. *See Minerva Surgical, Inc. v. Hologic, Inc.*, 59 F.4th 1371, 1377-78 (Fed. Cir. 2023) (finding reduction to practice because the invention was demonstrated in working prototypes that embodied the claims and because studies, along with documents describing the prototypes, demonstrated that it worked for its intended purpose); *Helsinn Healthcare S.A. v. Teva Pharms. USA, Inc.*, 855 F.3d 1356, 1372-74 (Fed. Cir. 2017) (reduction to practice of claimed formulation evidenced by a study report demonstrating efficacy of the drug, internal meeting

minutes acknowledging efficacy observed in a clinical study, and a press release that the study demonstrated efficacy). Regulatory approval or confirmation of clinical efficacy is not required to demonstrate that an invention works for its intended purpose. *See id.* at 1365-66.

Here, the method of improving exercise capacity in PH-ILD patients treated with iTre was reduced to practice well before April 2019. Drs. Hill, Waxman, Tapson, Saggar, and Channick all prescribed Tyvaso to PH-ILD patients using the dosing from the 2009 Tyvaso label and as recited in claim 1. *See supra* § V.A.1.a; FOF130, 119-122. Their real-world treatment resulted in observed improvements in their patients' exercise capacity, including through patient reported outcomes and measurable increases in 6MWD. *See supra* §§V.A.1.a-b; FOF119-120, 130. The actual treatment of PH-ILD patients with Tyvaso that resulted in actual improvements in exercise capacity demonstrate the invention of claim 1 was reduced to practice prior to April 2019.

2. Claims 1 and 17 Were Disclosed in Publications Such that a POSA Could Practice the Invention Prior to April 2019

"Ready for patenting" is also satisfied where an enabling disclosure provides sufficient detail for a POSA to practice the invention. *See Hamilton Beach Brands, Inc. v. Sunbeam Prods., Inc.*, 726 F.3d 1370, 1377-78 (Fed. Cir. 2013) (holding the invention was ready for patenting because detailed drawings and descriptions of the invention, which contained all limitations of the asserted patent, presented at meetings were sufficient to enable a POSA to practice the invention).

Here, as Dr. Hill explained, *Faria-Urbina* disclosed the use of iTre to treat PH-ILD patients using the same dosing in claim 1. FOF131. Dr. Waxman also testified that *Faria-Urbina* used the same dosing as in INCREASE, which is consistent with the dosing in claim 1, and that the PH-ILD patient population in his paper was the same as in the INCREASE study. FOF122, 131. In addition, *Faria-Urbina* reported that PH-ILD and CPFE patients' 6MWD improved by 21 and 55 meters, respectively, over three months. DTX505, 3-4; FOF24, 131. A POSA would be able to

follow the disclosure in *Faria-Urbina* prior to April 2019 and achieve the method of claims 1 and 17, further demonstrating those claims were reduced to practice. FOF131.

3. Hypothesis Generating Results Are Still Ready for Patenting

To the extent UTC argues that doctors' actual treatment and the disclosure of *Faria-Urbina* were merely "hypothesis generating" and thus not ready for patenting, they are incorrect. That a treatment generates "hypothesis generating" results means that it yielded positive results that lay the foundation for further research, not that the results were not ready for patenting. FOF132-133. Indeed, claim 9 of the '327 patent is directed to an FVC outcome, yet Dr. Nathan and his colleagues described the FVC results from INCREASE as "hypothesis generating." JTX1, 50; DTX9, 9; FOF133. That UTC sought and obtained a patent claim based on a "hypothesis generating" FVC result confirms that treatment of PH-ILD patients with Tyvaso and the disclosure in *Faria-Urbina* are sufficient to establish claims 1 and 17 were ready for patenting. FOF82.

C. The Prior Sale of Tyvaso Inherently Discloses Claims 5, 6, and 9

"[A] limitation or the entire invention is inherent and in the public domain if it is the 'natural result flowing from' the explicit disclosure of the prior art." *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1379 (Fed. Cir. 2003). To prove inherent anticipation, a party must show that, although the prior art does not explicitly disclose a feature of the invention, it "necessarily and inevitably" flows from practicing the prior art. *Id*. at 1378-79. There is no requirement that a POSA would have recognized the inherent disclosure at the time of the invention, *id.* at 1377, and "[e]xtrinsic evidence can be used to demonstrate what is 'necessarily present' in a prior art embodiment even if the extrinsic evidence is not itself prior art." *Hospira, Inc. v. Fresenius Kabi USA, LLC*, 946 F.3d 1322, 1329 (Fed. Cir. 2020). "If a product that is offered for sale inherently possesses each of the limitations of the claims, then the invention is on sale, whether or not the parties to the transaction recognize that the product possesses the claimed

characteristics." *Abbott Lab'ys*, 182 F.3d at 1319.

Applying this law, §VI.A, below, makes clear that the claims of the '327 patent only require one patient to experience the outcomes recited in claims 5, 6, and 9, not "virtually all" patients. That claim scope analysis applies equally to the inherent anticipation of claims 5, 6, and 9 based on the prior sale of Tyvaso to treat PH-ILD patients. Further, as relevant here, a commercially sold product or process that inherently meets all the limitations of a claim can invalidate that claim, even if the seller was unaware that the invention was present. *See, e.g., Abbott Lab'ys*, 182 F.3d at 1319; *Scaltech*, 269 F.3d at 1330-31 (finding the claimed process was on sale even though the seller did not recognize that it possessed the features later claimed).

Here, doctors treated PH-ILD patients using the standard dosing for Tyvaso, observed improvements in exercise capacity, and published those findings, all before April 2019. *See* FOF119-122, 129. The same drug, route of administration and dosing is disclosed in the later NEJM Paper for INCREASE. FOF134. The NEJM Paper establishes that using Tyvaso in PH-ILD patients with the dosing in claim 1 leads to the claimed NT-proBNP, exacerbations of ILD, and FVC outcomes claimed in claims 5, 6, and 9. FOF134. Because the doctors' prior treatment, *Faria-Urbina*, and the NEJM Paper all used the same drug, the same route of administration, the same dosing, and all in the same patient population, the NEJM Paper establishes that the prior sale of Tyvaso to treat PH-ILD will necessarily and inevitably result in at least one PH-ILD patient experiencing the outcomes claimed in claims 5, 6, and 9. FO134; *see infra* §§VI.A-B.

VI. CLAIMS 1, 5, 6, 9, AND 17 ARE INHERENTLY ANTICIPATED

A. The '327 Claims and the Legal Standard for Inherent Anticipation Do Not Require that "Virtually All" Patients Experience the Claimed Outcomes

As noted in §V.C above, a claim is inherently anticipated if the invention necessarily and inevitably flows from practicing the prior art. There is no requirement that a POSA recognized

the inherent disclosure at the time of the invention, and evidence post-dating the patent can be used to demonstrate what is necessarily present in the prior art.

As confirmed by this Court's construction of "a" or "the," the claims require only that one single patient achieve the claimed results to practice the claim. FOF135. The '327 patent does not claim a method of treatment in which "virtually all" patients benefit. *Id*. The law of inherent anticipation, including for method of treatment claims, holds that the prior art need only inherently anticipate what the inventors claimed—not more. *King Pharms., Inc. v. Eon Lab'ys, Inc*., 616 F.3d 1267, 1276 (Fed. Cir. 2010) ("To anticipate, the prior art need only meet the inherently disclosed limitation to the extent the patented method does."); *Arbutus Biopharma Corp. v. ModernaTX, Inc.*, 65 F.4th 656, 662, 664 (Fed. Cir. 2023). Because the '327 claims can be met by one patient, inherency here does not require that "virtually all" PH-ILD patients will necessarily and inevitably experience a claimed outcome, but only that following the 2017 Protocol will necessarily and inevitably result in at least one patient in the claimed PH-ILD population experiencing the claimed outcomes. Because the '327 patent claims do not recite limitations requiring a Phase 3 trial (FOF66), inherency does not require achieving the identical results as INCREASE. FOF135, 139.

UTC's "virtually all" argument runs afoul of the claims and misstates the law. No case holds that a prior art method cannot inherently anticipate method of treatment claim unless "virtually all" patients treated with the method would achieve the claimed results. Moreover, given interpatient variability, a method of treatment will lead to a distribution of outcomes across a patient population, with some patients who benefit differently, or not at all, compared to the overall population of treated patients. FOF136, 153-155.

King Pharms. examined the inherent anticipation of method of treatment claims that (as here) contained a single active dosing step (administering to the patient a therapeutically effective

amount of metaxalone with food) and a limiting preamble reciting the result (increasing bioavailability of metaxalone). *King Pharms.*, 616 F.3d at 1274; *see also King Pharms., Inc. v. Eon Lab'ys, Inc.*, 593 F. Supp. 2d 501, 506 (E.D.N.Y. 2009). Analogously, claim 1 of the '327 patent claims administering an effective amount of iTre according to the claimed dosage requirements with the result of improving exercise capacity. FOF6.

Critically, the evidence of inherency in *King Pharms.* was sufficient even though only some (i.e., not "virtually all") patients treated according to the prior art method actually experienced the claimed benefit of increased bioavailability. Indeed, the evidence showed that at least 9 of 42 patients did not experience the claimed benefit of taking metaxalone with food. *King Pharms.*, 593 F. Supp. 2d at 508-09. The patentee, like UTC here, argued no inherent anticipation because the evidence did not show that the prior art method led to the claimed result "each and every time." *Id*. The court rejected this argument because it would improperly hold "the prior art to a higher standard than the patent." *Id*. at 509; *see also King Pharms.*, 616 F.3d at 1275 (noting that the prior art method was inherently anticipated because it would lead to the claimed result in "most people."). The Federal Circuit affirmed, holding: "to inherently anticipate, the prior art need only give the same results as the patent, not better." *Id.* at 1276 (emphasis added). This case is also unlike *Galderma Lab'ys, L.P. v. Teva Pharm. USA, Inc.*, where the anticipatory reference did not disclose the same composition as the patent at issue. 799 F. App'x 838, 845-46 (Fed. Cir. 2020). Here, the 2017 Protocol discloses the exact same composition (Tyvaso) being used for exactly the same purpose (improving exercise capacity in a PH-ILD patient) as in the NEJM Paper.

In re Montgomery solidified the *King Pharms* legal standard. *See* 677 F.3d 1375, 1381-82 (Fed. Cir. 2012) (holding that prior-art publication of a clinical trial protocol for administration of ramipril to stroke-prone patients inherently anticipated a claim to a method of prevention of stroke

by administering compounds, including ramipril). Like the invalidating prior art in *King Pharms.* and *Montgomery*, the 2017 Protocol is not merely an abstract theory or invitation to investigate – it is "an advanced stage of testing designed to secure regulatory approval." *Id.* at 1382.

UTC's sole support for its purported "virtually all" requirement, *Glaxo Grp. Ltd. v. Kali Lab'ys, Inc.*, 2005 WL 1398507 (D.N.J. Jun. 10, 2005), falls apart under scrutiny. *Glaxo* is a district court case, did not involve a construction limiting the claims to "one or more," like here, and the prior art method and the claimed method were not the same: the prior art disclosed administration of ondansetron to "migraine sufferers, schizophrenics, the anxious, the obese, the manic, and others," whereas the claims at issue were focused solely on the new group of "those suffering from nausea." *Id*. at *3-4. The prior art did not inherently anticipate because it was not clear the prior art patient population included the claimed nausea-sufferers. *Id.* Thus, "virtually all" in *Glaxo* referred to the overlap in patient populations between the prior art and the challenged patent, not whether "virtually all" patients receiving the treatment would see a benefit. *Id.* Thus, *Glaxo* has no application here, where it is undisputed that the 2017 Protocol, INCREASE, NEJM Paper, and the '327 claims are all directed to the same PH-ILD population. FOF146-149. In accordance with the '327 claims and controlling law, inherent anticipation requires only one PH-ILD patient to necessarily and inevitably achieve the claimed outcomes.

B. The 2017 Protocol Inherently Anticipates Claims 1, 5, 6, 9 and 17

The 2017 Protocol inherently anticipates under the correct standard. On February 10, 2017, UTC published via clinicaltrials.gov a copy of its protocol for the INCREASE study. FOF137-138; DTX8. The results of the INCREASE study were published in the NEJM Paper after the '327 patent application was filed. FOF5, 55. Because those results were the necessary and inevitable result of the method of treatment disclosed in the 2017 Protocol, the 2017 Protocol inherently anticipates claims 1, 5, 6, 9 and 17. *See Hospira,* 946 F.3d at 1329.

The treatment of PH-ILD claimed in the '327 patent is not a new use of iTre, as compared to the method disclosed in the 2017 Protocol. The 2017 Protocol teaches the same drug, the same disease, the same route of administration, the same measurements/endpoints, and the same dosing as INCREASE, which led to the '327 patent. FOF140-152. The 2017 Protocol PH-ILD population would all have been included in INCREASE. *Id.* The only step of claim 1 is administering iTre to one PH-ILD patient to improve exercise capacity. That step is disclosed by the 2017 Protocol, and there is no difference between INCREASE, claim 1, and the 2017 Protocol. FOF150-155.

Although the 2017 Protocol does not provide results, recognition of the outcome in 2017 is not required for inherency. Instead, the results of INCREASE in the NEJM Paper show the necessary and inevitable result of performing the method in the 2017 Protocol is an increase in exercise capacity. FOF138, 153-155. These results also show the NT-proBNP, exacerbation, FVC, and 6MWD limitations of claims 5, 6, 9, and 17 were the natural result of the method disclosed in the 2017 Protocol. FOF156-159. These later results are sufficient to confirm that even if the 2017 Protocol, when performed, would not exactly match the results of INCREASE, it would necessarily and inevitably result in at least one patient achieving the claimed results in the '327 patent and thus inherently anticipates. *See King Pharms.*, 616 F.3d at 1275-76; FOF153-159.

UTC points to small differences to the inclusion criteria of the 2017 Protocol in the final INCREASE study, but the 2017 Protocol still necessarily and inevitably leads to the claimed results. The small changes decreased the minimum pulmonary vascular resistance criteria from ≥4 to >3 Wood Units; and decreased the minimum mean pulmonary arterial pressure from ≥30 to ≥25 mmHg. FOF148. UTC offered no evidence that minor differences in the carbon monoxide diffusion and maximum percent predicted FVC parameters would impact the outcome, and Dr. Channick testified they would not be expected to. *See id*. Either way, the entire population from

the 2017 Protocol is included in INCREASE because, as Dr. Channick testified, the 2017 Protocol was more stringently defined. FOF146-149. *See Arbutus Biopharma*, 65 F.4th at 664 (finding inherent anticipation where prior art "similar[ly] disclose[d]" the claimed invention). Every PH-ILD patient who would have qualified for the 2017 Protocol would also have been included in INCREASE, and the average hemodynamic parameters of the patients that actually participated in INCREASE significantly exceeded even the more stringent criteria of the 2017 Protocol. FOF149.

Similarly, UTC's argument that there was a relevant difference in dosing between the 2017 Protocol and INCREASE is wrong. Dr. Nathan conceded that by 2017 doctors knew from the Tyvaso label that therapy "should begin with three breaths of Tyvaso"; Dr. Hill testified that this behavior was widely known, including by Dr. Waxman who helped write the 2017 Protocol, and that a POSA would know that titrating up to a maximum of 12 breaths includes each breath interval between 3 and 12. FOF152. Thus, doctors running the 2017 Protocol would have administered treprostinil on the same dosing schedule used in INCREASE and recited in the claims.

Dr. Nathan's rebuttal that these differences mean it is impossible to predict the outcome of the 2017 Protocol cannot be credited. Inherency is found where, as here, the same formulation is used (Tyvaso), and "almost identical wording" between the prior art, the disclosed results, and the claimed invention, are present. *Arbutus Biopharma*, 65 F.4th at 663-64. It is simply not credible that if the 2017 Protocol was followed, not a single patient would achieve the limitations of claims 1, 5, 6, 9, and 17. Further, this is contradicted by Dr. Nathan's infringement testimony, where he assumes that PH-ILD patients (regardless of their specific hemodynamic, FVC, and other measures) treated with Yutrepia will experience the claimed results even if their outcomes are never measured—based solely on the same NEJM Paper. FOF9, FOF136-139. UTC's entire rebuttal to inherent anticipation is in irresolvable conflict with its infringement arguments. If, as

UTC argues, dosing even a different formulation of iTre than in INCREASE today with the claimed methods leads to infringement, then it is equally true that using the same dosing schedule of Tyvaso, the same iTre formulation used in INCREASE, as disclosed in the 2017 Protocol necessarily and inevitably leads to one patient achieving the limitations of the claims. UTC also demands that inherent anticipation requires actual test results from prior art patients, but that too would "require actual tests … to prove any single act of infringement." *See King Pharms*., 593 F. Supp. 2d at 509. UTC's contradictory standards for infringement and inherent anticipation violates "the bedrock principle of 'that which infringes if later, anticipates if earlier.'" *Id*., (citing *SmithKline Beecham Corp. v. Apotex Corp*., 439 F.3d 1312, 1321 (Fed. Cir. 2006)).

INCREASE was, at most, a set of measurements confirming the natural result flowing from treating PH-ILD patients with iTre, rendering the claims inherently anticipated. FOF153-155. Per *King Pharms.*, "[t]o hold otherwise would remove from the public a method of treating [PH-ILD] that has been performed for [over a decade]" by doctors. 616 F.3d at 1276 (citing *Atlas Powder Co. v. Ireco, Inc*., 190 F.3d 1342, 1348 (Fed. Cir. 1999)) ("The public remains free to make, use, or sell prior art compositions or processes. . . . The doctrine of anticipation by inherency, among other doctrines, enforces that basic principle.")). For these reasons, and as demonstrated by the NEJM Paper, the 2017 Protocol inherently anticipates claims 1, 5, 6, 9, and 17.

VII. CLAIM 9 LACKS WRITTEN DESCRIPTION SUPPORT

Claim 9 is invalid because the written description does not convey the inventors possessed the full scope of the claim. *See Ariad Pharms. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc); *Nuvo Pharms. v. Dr. Reddy's Lab'ys*, 923 F.3d 1368, 1376-77 (Fed. Cir. 2019).

A. Full Scope of Claim 9 Requires a Statistically Significant Increase of Both Absolute and Percent Predicted FVC in the Full PH-ILD Population

Claim 9's scope requires a statistically significant increase in both absolute and percent

predicted FVC. *First*, the words of the claim itself do not limit the claim to just absolute ***or*** percent predicted, and the patent clearly references both in the specification and Tables 1-3 and 10. FOF160-163. *Second*, by its express terms, claim 10 depends from claim 9 and is limited to a measure of absolute FVC only. FOF162. Claim 9 thus must include both absolute and percent predicted FVC improvements within its full scope. *See, e.g.*, *Littelfuse, Inc. v. Mersen USA EP Corp.*, 29 F.4th 1376, 1380 (Fed. Cir. 2022) ("if a dependent claim reads on a particular embodiment of the claimed invention, the corresponding independent claim must cover that embodiment as well"). *Third*, the inventors expressed no preference for percent predicted FVC and instead discussed them equally. FOF162. *Fourth*, as recognized at the pretrial conference, there is no dispute that claim 9 "encompasses" both absolute and percent predicted FVC. FOF161.

At the outset, Dr. Wertheim's opinions should be discounted because they are based on his construction that claim 9 encompasses only percent predicted FVC. *See Phillips v. AWH*, 415 F.3d 1303, 1318 (Fed. Cir. 2005) (en banc). In an effort to shore up his construction, Dr. Wertheim opined that a POSA would have a preference for percent predicted FVC. FOF163. However, neither the claims nor the specification support any such preference. FOF162. Moreover, UTC's experts can't agree on this point—Dr. Nathan contradicted Dr. Wertheim and testified that a POSA would have a preference for absolute, not percent predicted, FVC. FOF163. Indeed, Dr. Wertheim ultimately conceded that claim 9 covers "either" absolute or percent predicted, which means its full scope covers both. *Id.*

Claim 9 also requires written description support for a statistically significant FVC improvement in the full PH-ILD population after 8, 12, or 16 weeks. The sole experimental data, Tables 1-3 and 10, confirms that a statistically significant improvement in absolute FVC was <u>not</u> achieved in the full intent-to-treat population ("ITT"). FOF166, 168-171. And this ITT population

is the only data corresponding to the full scope of the PH-ILD population of claim 9. FOF164-165. The experts agree that the patients reflected in Tables 2 and 3 are only a subset of the total PH-ILD population of Table 1 and Table 3 is "a subgroup of a subgroup." FOF166, 170-171. Claim 9 requires support for a statistically significant improvement in both absolute and percent predicted FVC in the full claimed PH-ILD population after the claimed timepoints. FOF164-171.

B. The Written Description Fails to Support the Full Scope of Claim 9

The written description fails to convey that the inventors possessed the full scope of what they claimed – a statistically-significant increase in FVC as measured by both absolute and percent predicted values in the full PH-ILD population. *See Biogen Int'l GmbH v. Mylan Pharms.*, 18 F.4th 1333, 1343 ("when the inventor expressly claims [a] result, our case law provides that [such] result must be supported by adequate disclosure in the specification"); *Nuvo*, 923 F.3d at 1384. Table 1 demonstrates that the ITT population *did not* experience a statistically significant improvement in absolute FVC. FOF169. Table 1 confirms that a statistically significant percent predicted FVC improvement does not necessarily correspond with a statistically significant absolute FVC improvement in the "same breath." FOF162, 169. No part of the specification conveys the inventors possessed a statistically significant improvement in both absolute and percent predicted FVC in the full ITT population. Thus claim 9's full scope lacks written description support. *See Juno Therapeutics v. Kite Pharma, Inc.*, 10 F.4th 1330, 1337 (Fed. Cir. 2021) ("the written description must lead a person of ordinary skill in the art to understand that the inventors possessed the entire scope of the claimed invention") (emphasis added).

Dr. Wertheim pivots, relying on subpopulation data in Tables 2 and 3, denoting a statistically significant improvement in percent predicted and absolute FVC (week 16 only). FOF163, 170-171. But Tables 2 and 3 are only subgroups of the total PH-ILD population of claim 9. FOF170-171. Description of a mere subset of the full scope of claim 9's PH-ILD

population is not enough. *See Ariad Pharms.*, 598 F.3d at 1352-53 ("[t]he written description requirement also ensures that when a patent claims a genus by its function or result, the specification recites sufficient materials to accomplish that function—a problem that is particularly acute in the biological arts."). Additionally, Tables 2 and 3 provide no evidence of any statistically significant improvement in percent predicted or absolute FVC after 12 weeks. FOF170-171. Accordingly, support only for a subpart of the full claim scope is insufficient to save claim 9.

Finally, the law is settled that mere *ipsis verbis* is not sufficient to establish written description when data in the specification proves otherwise. FOF162-163, 169-171; *Nuvo*, 923 F.3d at 1380 ("We have expressly rejected the 'argument that the written description requirement ... is necessarily met as a matter of law because the claim language appears in *ipsis verbis* in the specification.'"). For the reasons herein, claim 9 is invalid for lack of written description support.

VIII. CONCLUSION

Liquidia asks this Court to find claims 1, 5, 6, 9, 14, and 17 of the '327 patent, which are limited to PH-ILD invalid. In the event that the Court concludes otherwise, any proposed relief for UTC under 21 U.S.C. § 271(e)(4)(A) or (B) may not, as a matter of law, impact or otherwise restrict the approval and commercial marketing of Yutrepia for PAH—an indication that, without question, is not covered by the asserted claims of the '327 patent and cannot be "involve[d] in the infringement."

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